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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/825,757	04/16/2004	Jeffrey M. Linnen	GP146-04.UT	8545

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EXAMINER	
SALMON, KATHERINE D	
ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
11/06/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/825,757	LINNEN ET AL.	
	Examiner	Art Unit	
	Katherine Salmon	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *116-119,124-134 and 139-181* is/are pending in the application.

4a) Of the above claim(s) *131-134,139-144 and 153-174* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *116-119,124-130,145-152 and 178-181* is/are rejected.

7)☒ Claim(s) *178-181* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed 8/17/2007.

2. Claims 116-119, 124-134, and 139-181 are pending. Claims 1-115, 120-123, and 135-138 are cancelled. Claims 131-134, 139-144, and 153-174 are withdrawn as being drawn to a nonelected invention.

3. This action contains rejections for Claims 116-119, 124-130, 145-152, and 178-181 as necessitated by amendment or reiterated. Response to arguments follows.

4. This action is FINAL.

Rejections Necessitated by Amendment or Reiterated

Priority

5. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Application No. 60/469294, 60/465428, 60/464049, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The applications fail to disclose SEQ ID No. 3, 24, or 25, therefore there does not appear to be support for the applicant's presently claimed invention in these provisional applications. As a result the earliest filing date of record is deemed to be 4/16/2004.

Response to Arguments

The reply did not traverse the denial of priority to the prior-filed applications, Application No. 60/469294, 60/465428, 60/464049. Therefore the filing date of record is being maintained as 4/16/2004.

Claim Objections

6. Claims 178-181 are objected to because of the following informalities: Claims 178-181 need to be amended to include all limitations because Claims 178-181 depend from claims which have been withdrawn (e.g. Claims 121, 166, and 162). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 116-119, 124-130, and 176-177 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 116-119, 124-130, and 176-177 are indefinite over the phrase "perfectly complementary to all or a portion of a target sequence consisting of the base sequence of SEQ ID No. 3 or its complement" in lines 4-5 of Claim 116. It is not clear if all of the target sequence consists of SEQ ID NO. 3 or its complement or if only a portion of the target sequence consists of SEQ ID No. 3 or its complement. Therefore it is unclear which nucleic acids are including in a target sequence, which consists of SEQ ID No. 3. It is unclear if more than just the nucleic acids of SEQ ID NO. 3 are encompassed by the claim language. As such the metes and bounds of the claims are unclear and therefore it is not clear if the probe's target binding portion needs to comprise all of SEQ ID NO. 3 or a portion.

Claims 116-119, 124-130, and 176-177 are indefinite over the phrase "perfectly complementary to all or a portion of a target sequence consisting of the base sequence of SEQ ID No. 3 or its complement" in lines 4-5 of Claim 116. It is indefinite because if the probe were perfectly complementary to the complement of SEQ ID No. 3 then it would encompass SEQ ID No. 3 because a probe complementary to the complement of SEQ ID No. 3 would be SEQ ID No. 3.

Claims 117-119 are drawn to a probe comprising a target binding portion comprising at least 10, at least 15, or at least 18 contiguous base region perfectly complementary to at least 10 contiguous base region of SEQ ID No. 3. However in the

independent claim 116 which Claim 117 depends from, the probe comprises a target binding portion that is perfectly complementary to all or a portion of a target sequence consisting of SEQ ID NO. 3. Therefore Claim 116 is drawn to a probe that comprising at least all the nucleotides in SEQ ID NO. 3, it is unclear therefore if the probe would comprise less than all the nucleotides in SEQ ID NO. 3 because Claim 116 requires that the probe comprises all 23 nucleic acid bases from SEQ ID NO. 3.

Claims 124-125 are drawn to a probe comprising a target-binding portion comprising a portion of SEQ ID No. 3 or a sequence complementary to 18 to 23 contiguous bases of SEQ ID No. 3. However in the independent claim 116, which Claim 117 depends from, the probe comprises a target binding portion that is perfectly complementary to all or a portion of a target sequence consisting of SEQ ID NO. 3. Therefore Claim 116 is drawn to a probe that comprising at least all the nucleotides in SEQ ID NO. 3, it is unclear therefore if the probe would comprise less than all the nucleotides in SEQ ID NO. 3 because Claim 116 seems to require that the probe comprises all 23 nucleic acid bases from SEQ ID NO. 3.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 116-119, 124-130, 145 and 175-181 are rejected under 35 U.S.C. 103(a) as being unpatentable over Genbank Accession Number NC_004718.1 (NCBI GenBank Accession Number April 14, 2003) in view of Peiris et al. (US Patent Application Publication 2005/0009009 A1 January 13, 2005).

GenBank Accession Number NC_004718 (April 14, 2003) discloses the complete genomic sequence of the SARS coronavirus. With regard to Claims 116-119, 124, 145, 175, and 178-181, NC_004718 discloses a sequence in which SEQ ID No. 3, 24, and 25 are contained within. SEQ ID No. 3 is identical to nucleotides 18162-18206. SEQ ID No. 24 is identical to nucleotides 18243-18273. SEQ ID No. 25 is identical to nucleotides 18162-18206. Therefore, NC_004718 discloses a sequence, which comprises the SEQ IDs in the claimed invention.

NC_004718, however, does not teach the specific fragments of SEQ ID Nos. 3, 24, 25 for detection of the SARS virus, labels, or a kit.

Peiris et al. teaches the use of oligonucleotides for a diagnostic assay for detecting SARS.

With regard to Claims 116-119, 124-126, 145, 175-177, and 178-181, Peiris et al. teaches a methodology to produce oligonucleotides to detect the SARS virus. Peiris et al. teaches primers for use in amplifying the mRNA or genomic RNA of the SARS virus is based on known synthesizing methods (p. 7 paragraph 58). Peiris et al. teaches the exact length of primer will depend on the temperature, buffer, and nucleotide composition (p. 7 paragraph 58). Peiris et al. teaches the primer must prime the synthesis of extension products in the presence of the inducing agent for amplification (p. 7 paragraph 58).

Peiris et al. teaches primers and probes for polynucleotides of the SARS virus can be developed using known methods (p. 7 paragraph 59). Peiris et al. teaches primers are preferred to be as close as possible to the probe without overlapping the probe (p. 7 paragraph 59). Peiris et al. teaches the G-C content of the primers should be in the 20% to 80% range (p. 7 paragraph 59). Peiris et al. teaches it is preferred to avoid runs of an identical nucleotides especially guanine (p. 7 paragraph 59). Peiris et al. teaches the preferred melting temperature of each primer is 58 to 60 (p. 7 paragraph 59). . Peiris et al. teaches the five nucleotides at the 3' end of each primer is preferred to not have more than two G or C bases (p. 7 paragraph 59). Peiris et al. teaches probes can be designed using software such as Primer Express (p. 7 paragraph 60).

Peiris et al. teaches it is preferable to keep the G-C content in the 20%-80% range and to avoid runs of an identical nucleotide (p. 7 paragraph 60)/

Peiris et al. teaches the size of the primers used to amplify a portion of the mRNA is at least 10, 15, 20, 25, or 30 nucleotides in length (p. 7 paragraph 62).

Peiris et al. teaches that besides the SARS virus there are two known serogroups of human cornoviruses (229E and OC43) (p. 27 paragraph 251). Peiris et al. teaches the primer sets used in the present assay do not have homology to either of the strains so therefore they do not cross-react with the strains (p. 27 paragraph 251). Further, Peiris et al. teaches the sequence analyses of the available sequences in regions of the OC43 polymerase gene indicate the SARS virus is genetically distinct from OC43 (p. 27 paragraph 251).

Peiris et al. teaches using nucleotides in a RT-PCR to detect SAS virus (Abstract). Peiris et al. teaches making primers and probes based on the genomic sequence of hSARS virus to use in TaqMan assays (Abstract). With regard to Claims 127-129, Peiris et al. teaches the probe is a Taqman probe, which consists of an oligonucleotide with a 5'reporter (luminescent) dye and a 3' quencher dye (a pair of interacting labels consisting of a luminescent and a quencher in which the probe is detectably labeled) (p. 6 paragraph 54).

With regard to Claim 130, Peiris et al. teaches using hybridization conditions which are stringent conditions and include a temperature ranging from 50°C to 65°C (this range includes 60°C) (p. 3 paragraph 26).

With regard to Claim 175, Peiris et al. teaches oligonucleotide-based kits comprising a detectably labeled oligonucleotide, which hybridizes to the sequence of the SARS virus and a pair of primers to amplify the nucleic acid molecule (p. 8 paragraph 65).

Therefore, the ordinary artisan would have been motivated to select any number of oligonucleotides including SEQ ID No. 3, 24, and 25 for amplifying and detecting the SARS virus. The art of designing probes and primers at the time the invention was made was very well described in the art. The art uses alignment programs to align sequences of interest and then uses algorithms to select and test probes and primers for their desired function of either detecting or distinguishing particular organisms. Designing primers and probes, which are equivalents to those taught in the art, is routine experimentation. The prior art is replete with guidance and information necessary to permit the ordinary artisan in the field of nucleic acid detection to design primers and probes. The claimed primers are prima facie obvious over the cited references in the absence of secondary considerations, given the extensive teachings in the art. It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use the SARS sequence as disclosed by NC_004718 to create new oligonucleotides to detect the SARS virus using the guidance of the design constraints as taught by Peiris et al. to obtain equivalent alternative oligonucleotides of the claimed invention such as SEQ ID No. 25 and 24. The ordinary artisan would be motivated to have designed and tested new oligonucleotides from

fragments of NC_004718 to obtain additional oligonucleotides that function to detect the SARS virus and identify oligonucleotides with improved properties.

Response to Arguments

The reply traverses the rejection. The reply asserts that Example 1 of the specification illustrates the unexpected benefits of the claimed probes (p. 15 1st full paragraph). The reply asserts that example 1 illustrates the unexpected benefits of the claimed probes because probes having target binding portions that overlap with 3' and 5' end portions of SEQ ID No. 3 did appreciably hybridize to amplicons containing the complement of SEQ ID No. 3 (p. 15 1st full paragraph). The reply asserts that the specification points to probes 44 and 45 as showing exhibited specificity (p. 15 1st full paragraph). The reply asserts that the amplification oligonucleotides of the claimed invention had higher sensitivity than the amplification reactions of Peiris (p. 15 last paragraph). The reply asserts that Peiris amplification reactions are not as sensitive and depend on sample size, RNA extraction protocol, and method of amplification (p. 15 last paragraph).

These arguments have been fully considered but have not been found persuasive.

In the instant case it is clear that the prior art teaches the critical parameters necessary for probe selection including the preferred sequence regions and methodology to select probes which doe no cross react with similar viruses such as 229E and OC43, and a sequence which spans the region of interest (p. 27 paragraph

251). Therefore, the prior art provides the information necessary to select probes and the prior art provides a reasonable expectation of success that every probe would function in a detection assay. This is not just general guidance because the prior art provides specific guidance regarding the selection of probes for the specific detection of the SARs virus without cross-reactivity to human cornoviruses. Therefore there is a reasonable expectation of success in designing probes without secondary considerations that the claimed probes have unexpected results.

The reply seems to be pointing to support in the specification for unexpected results. The reply points to SEQ ID No. 44 and 45 as probe, which exhibits specificity for the target sequence. However, the claims are not limited to SEQ ID NO. 44 and 45, but rather a probe comprising SEQ ID No. 3 or its complement. The specification has not provided any guidance that such probes would have a higher degree of specificity to detect the SARS virus than other equivalent probes. Additionally the reply points to the high sensitivity of the probes in Example 1 and 2 compared to the sensitivity of the probes of Peiris et al. It is again noted that the probes claimed are not limited the specific probes used in the detection assay of Example 1 and 2 but rather probes comprising SEQ ID No. 3.

As to the assertion that the sensitivity of the probes in Example 1 and 2 are more sensitive than the probes of Perris et al. the reply points to the rationale of Peiris et al. that sensitivity is affected by sample size, RNA extraction protocol and method of amplification. However, the claims are drawn to probe products and not amplification assays. Therefore, the reduced sensitivity of the probes of Peiris et al. stems from

amplification parameters and not the composition of the probe structure.

As such, applicant has not provided evidence via secondary consideration that the probes made by the suggestion and teachings of the prior art would not be equivalent structures as the claimed probes. This should not be construed as an invitation for providing evidence. As further stated in the MPEP 716.01 regarding the timely submission of evidence:

A) Timeliness.
Evidence traversing rejections must be timely or seasonably filed to be entered and entitled to consideration. In re Rothermel, 276 F.2d 393, 125 USPQ 328 (CCPA 1960). Affidavits and declarations submitted under 37 CFR 1.132 and other evidence traversing rejections are considered timely if submitted:
(1) prior to a final rejection,
(2) before appeal in an application not having a final rejection, or
(3) after final rejection and submitted
(i) with a first reply after final rejection for the purpose of overcoming a new ground of rejection or requirement made in the final rejection, or
(ii) with a satisfactory showing under 37 CFR 1.116(b) or 37 CFR 1.195, or
(iii) under 37 CFR 1.129(a).

10. Claims 146-152 are rejected under 35 U.S.C. 103(a) as being unpatentable over Genbank Accession Number NC_004718.1 (NCBI GenBank Accession Number April 14, 2003) in view of Peiris et al. (US Patent Application Publication 2005/0009009 A1 January 13, 2005) as applied to Claims 116-119, 124-130, 145 and 175-181 above and further in view of McDonough et al. (US Patent 5766849 June 16, 1998).

Neither GenBank Accession Number NC_004718.1 nor Peiris et al. teaches a RNA polymerase such as the T7 promoter region on an oligonucleotide.

With regard to Claims 146-152, McDonough et al. teaches oligonucleotides complementary to a target sequence wherein the 5' region complexes with a promoter for an RNA polymerase (Column 6 lines 60-66). McDonough et al. teaches the RNA polymerases include t& (Column 6 line 13).

Therefore it would have been prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the oligonucleotides of Genbank Accession Number NC_004718.1 (NCBI GenBank Accession Number April 14, 2003) in view of Peiris et al. to include a T7 polymerase at the end of the oligonucleotides as taught by McDonough et al. The ordinary artisan would be motivated to attach a T7 polymerase to the end of an oligonucleotide because McDonough et al. teaches using polymerase on the end of one oligonucleotide in an assay enhances the efficiency of the specific amplification reaction (Column 7 lines 10-15). McDonough et al. teaches the presence of T7 on the end of an oligonucleotide reduces the efficiency of formation of byproducts such as primer-dimers and therefore enhances amplification efficiency (Column 10 lines 50-53). The ordinary artisan would be motivated to include a RNA polymerase and an RNA promoter region on one of the oligonucleotides in order to increase the detection assay efficiency by reducing the ability of the oligonucleotides to form primer-dimers.

Response to Arguments

The reply traverses the rejection. The reply asserts that the limitation of a detection probe comprising a target binding portion comprising a target binding portion complementary to all of a portion of a target sequence consisting of the base sequence

of SEQ ID No. 3 or its complement (p. 16 2nd paragraph) is not taught by Genbank Accession No. NC_004718.1 in view of Peiris et al. and McDonough et al. However, as discussed in the response to Arguments section in the 35 USC 103(a) rejection of Genbank Accession No. NC_004718.1 in view of Peiris et al. the combination of references suggest making probes, which are equivalents to claimed probes.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katherine Salmon whose telephone number is (571) 272-3316. The examiner can normally be reached on Monday-Friday 8AM-430PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Katherine Salmon
Examiner
Art Unit 1634

/Jehanne Sitton/
Primary Examiner
10/26/2007